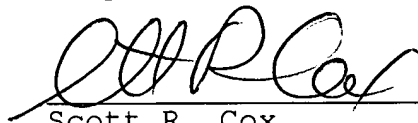


CONCLUSION

The applicant asserts that all claims, as amended, are now allowable. All rejections under 35 USC §102 have been overcome by the amendments to the claims. The rejection under 35 USC §103 has also been overcome by the amendments to the claims, as well as the proof of secondary considerations, including long felt but unresolved need and the teaching in the art against the solution proposed by the applicant. The applicant respectfully requests that all claims be allowed. If there are any further questions concerning this Preliminary Amendment, please contact applicant's counsel.

Respectfully submitted,



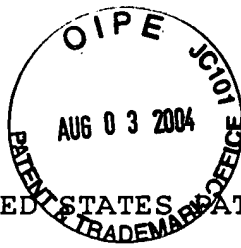
\_\_\_\_\_  
Scott R. Cox  
Reg. No. 31,945  
LYNCH, COX, GILMAN & MAHAN, P.S.C.  
400 West Market Street, Suite 2200  
Louisville, Kentucky 40202  
(502) 589-4215

CERTIFICATE OF SERVICE

I hereby certify that this correspondence is being deposited with the United States Postal Service in an envelope as Express Mail Post Office to Addressee," mailing Label Number EU760105634US, envelope addressed to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: August 2, 2004 Nelly Hart

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: :  
Jon M. Miller :  
Serial No.: 09/280,279 :  
Filed: March 29, 1999 : Group No. 1617  
Attorney Docket No.: P-1109 : Examiner: Shahnam J.  
Sharareh  
For: PREVENTION OR REVERSAL OF : Confirmation No. 5533  
WEIGHT GAIN ASSOCIATED WITH :  
THE USE OF ANTIPSYCHOTIC OR :  
MOOD STABILIZING DRUGS BY :  
OF THE USE OF HISTAMINE H<sub>2</sub>- :  
RECEPTOR ANTAGONISTS :

MAIL STOP RCE  
Commissioner for Patents  
P.O. BOX 1450  
Alexandria, VA 22313-1450

AFFIDAVIT UNDER 37 CFR 1.132

Dr. Jon M. Miller, being duly sworn, does hereby depose and state as follows:

1. That I received a Doctors degree in Medicine from the University of Oklahoma on June 2nd of 1991.

2. That I am the inventor of patent application Serial No. 09/280,279, filed on March 29, 1999 entitled "PREVENTION OR REVERSAL OF WEIGHT GAIN ASSOCIATED WITH THE USE OF ANTI-PSYCHOTIC OR MOOD STABILIZING DRUGS BY MEANS OF THE USE OF HISTAMINE H<sub>2</sub> RECEPTOR ANTAGONISTS."

3. That I have been employed as a psychiatrist since 1992.

4. That I have reviewed the Office Action from the United States Patent and Trademark Office dated April 6, 2004, the Article titled Histamine H<sub>2</sub>-receptor Antagonists in Schizophrenia, Rosenberg, et al., U.S. Patent No. 5,897,910, and WO 92/00736.

5. It is my opinion that there has been a long felt, but unresolved need, for a resolution of the weight gain problem for patients that often occurs during the use of antipsychotic or mood altering drugs. In fact, there have been over two hundred papers in the medical literature written during the period of 1999 - 2004 dealing with some aspect of weight gain and/or other metabolic changes, such as hyperlipidemia, associated with the use of atypical antipsychotics. Further, the FDA recently compelled the manufacturers of all atypical antipsychotics to place a warning in their package inserts about potential diabetes mellitus risks. Such risks are often caused by weight gain.

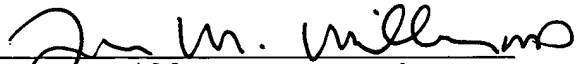
6. At this time there is no accepted or proposed method for prevention of weight gain outside of restricting caloric intake and increasing exercise. For clinical reasons, even diet and exercise are not viable means of weight loss in most persons taking antipsychotics. The "metabolic syndrome" (weight gain, diabetes, hyperlipidemia, etc.) associated with the use of atypical antipsychotics is life threatening and yet no suitable treatment has been found.

7. Accordingly, it was a surprising result to me that the utilization of histamine H<sub>2</sub> antagonists with antipsychotic or mood altering drugs resulted in elimination or reduction of the weight gain that was normally associated with the utilization of these antipsychotic or mood altering drugs.

8. It is my view that my proposed solution to the problem of weight gain associated with the utilization of atypical antipsychotics has not been accepted, even by those skilled in the art. In 1999, I submitted a "letter to the editor" to the Journal of Clinical Psychiatry describing three case studies of patients receiving histamine H<sub>2</sub> antagonists for gastroesophageal reflux disorder who did not demonstrate weight gain while also taking olanzapine and suggested that this might be a useful treatment for atypical antipsychotic-induced weight gain. My proposed concept was rebuked by the reviewer who stated that "the conclusion of the authors that famotidine stabilizes the weight gain of these people is incorrect at best... the rationale of adding an H<sub>2</sub> antagonists to a drug that authors are saying has substantial H<sub>2</sub> antagonism makes no sense." Thus, a person skilled in the art reviewing my proposed concept did not accept and in fact rejected this very concept. In contrast, I have surprisingly discovered that the combination of these two drugs can result in significant reduction in the weight gain commonly associated with the use of atypical antipsychotics.

9. I have reviewed the patent by Dr. Stoa-Birketvedt. I note that she cites two patents from 1979 (Vivino and Ritter) which attempt to use a histamine H<sub>2</sub> antagonist as an aid in facilitating weight loss. She acknowledges that there had been no subsequent publications to support or confirm these suggestions as of 1990. This indicates to me that there was no success in the use of these drugs as a weight loss agent. Further, Dr. Stoa-Birketvedt's patent teaches that cimetidine must be used under a strict regime, requiring many additional steps including: 1) the addition of dietary fiber to the patient's diet, 2) moderate exercise, 3) low caloric intake and 4) good nutrition to result in weight loss. Because of the requirement of low caloric intake, moderate exercise, and dietary fiber, it is not clear from this article what caused the weight loss. Notwithstanding the supposed disclosures of this reference, to my knowledge, there has been no clinical or commercial use of the combination of drugs proposed in my application. In my view the failure of the method of the Stor-Birketvedt patent to be utilized implies that the approach was not successful and therefore teaches against the combination of a histamine H<sub>2</sub> antagonist with an antipsychotic drug to induce weight loss.

Further, affiant saith not.

  
Jon M. Miller, M.D., PhD.

STATE OF KENTUCKY     )  
                                      ) SS  
COUNTY OF JEFFERSON )

Acknowledged, subscribed and sworn to before me this 28<sup>th</sup> day  
of July, 2004, by Jon M. Miller, M.D., PhD. to be his act  
and deed.

My commission expires: April 9, 2005  
  
NOTARY PUBLIC, STATE AT LARGE, KY

SRC:hh  
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